REVIEW

Benzene in the environment: an assessment of the potential risks to the health of the population

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Abstract

***Objectives*—Benzene has long been recognised as a carcinogen and recent concern has centred on the effects of continuous exposure to low concentrations of benzene both occupationally and environmentally. This paper presents an overview of the current knowledge about human exposure to benzene in the United Kingdom population based on recently published data, summarises the known human health effects, and uses this information to provide a risk evaluation for sections of the general United Kingdom population.**

***Method*—Given the minor contribution that non-inhalation sources make to the overall daily intake of benzene to humans, only exposure from inhalation has been considered when estimating the daily exposure of the general population to benzene. Exposure of adults, children, and infants to benzene has been estimated for different exposure scenarios with time-activity patterns and inhalation and absorption rates in conjunction with measured benzene concentrations for a range of relevant microenvironments. Exposures during refuelling and driving, as well as the contribution of active and passive tobacco smoke, have been considered as part of the characterisation of risk of the general population.**

***Results*—Infants (<1 years old), the average child (11 years old), and non-occupationally exposed adults, receive average daily doses in the range of 15–26, 29–50, and 75–522 μg of benzene, respectively, which correspond to average ranges to benzene in air of 3.40–5.76 μg/m^3, 3.37–5.67 μg/m^3, and 3.7–41 μg/m^3 for infants, children, and adults, respectively. Infants and children exposed to environmental tobacco smoke have concentrations of exposure to benzene comparable with those of an adult passive smoker. This is a significant source of exposure as a 1995 United Kingdom survey has shown that 47% of children aged 2–15 years live in households where at least one person smokes. The consequence of exposure to benzene in infants is more significant than for children or adults owing to their lower body weight, resulting in a higher daily intake for infants compared with children or non-smoking adults. A worst case scenario for exposure to benzene in the general population is that of an urban smoker who works adjacent to a busy road for 8 hours/day—for example, a maintenance worker—who can receive a mean daily exposure of about 820 μg (equal to an estimated exposure of 41 μg/m^3). The major health risk associated with low concentrations of exposure to benzene has been shown to be leukaemia, in particular acute non-lymphocytic leukaemia. The lowest concentration of exposure at which an increased incidence of acute non-lymphocytic leukaemia among occupationally exposed workers has been reliably detected, has been estimated to be in the range of 32–80 mg/m^3. Although some studies have suggested that effects may occur at lower concentrations, clear estimates of risk have not been determined, partly because of the inadequacy of exposure data and the few cases.**

***Conclusions*—Overall the evidence from human studies suggests that any risk of leukaemia at concentrations of exposure in the general population of 3.7–42 μg/m^3—that is at concentrations three orders of magnitude less than the occupational lowest observed effect level—is likely to be exceedingly small and probably not detectable with current methods. This is also likely to be true for infants and children who may be exposed continuously to concentrations of 3.4–5.7 μg/m^3. As yet there is no evidence to suggest that continuous exposures to these environmental concentrations of benzene manifest as any other adverse health effect.**

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Benzene is a well known genotoxic carcinogen and has caused great concern historically as an occupational health hazard. Progressive reduction in use of benzene and continual reduction in the occupational exposure limits has ensured that effects due to high concentrations of benzene in the workplace should no longer present a serious problem except in the case of

accidents. Current concern is centred on the effects of long term continuous low concentrations of exposure to benzene both occupationally and environmentally.

Benzene is a simple cyclic organic compound which is found naturally in the environment at low concentrations. Benzene occurs naturally in crude oil and as a consequence is a constituent of petrol. It is also formed during incomplete combustion of fossil fuels (petroleum products, coal, and to a lesser extent, wood). Also, it is a commercially important intermediate in the manufacture of many chemicals.[1]

In the past, benzene was widely used as a solvent, mainly in industrial paints, paint removers, adhesives, degreasing agents, denatured alcohol, rubber cements, and arts and crafts supplies.[2 3] The imposition of increasingly lower occupational exposure limits and more stringent legislation has led to a reduction in these uses, with, currently, only 0.74% of benzene being used as a solvent in the United Kingdom, mainly as a laboratory reagent.[3] There is a wide range of sources of potential very low concentrations of benzene in homes. For example, building materials and certain furnishing materials may contain residual concentrations of benzene.[4] Other potential sources include environmental tobacco smoke, photocopier and laser printed paper, particle board furniture, floor adhesives, paints, wood panelling, caulking, and paint remover.[5]

Emissions to air increased significantly in the period 1960–90 as a consequence of the rapid increase in vehicle numbers. During 1995, an estimated 35 kilotonnes of benzene were emitted to the United Kingdom environment. Some 70% of emissions are currently derived from road transport, mainly from petrol[6]; the most important sources include evaporative losses, refuelling emissions, and combustion of petrol.

The aim of this paper is to give an overview of the available data from the United Kingdom on environmental exposure to benzene from all sources in the general population, to summarise the known health effects, and to use this information to evaluate any potential risk to human health. The paper summarises an extensive report produced by the Institute for Environment and Health.[7]

Human health effects due to exposure to benzene

Numerous reviews over the years have described and evaluated adverse health effects associated with exposure to benzene.[2 8–13] However, all of these effects were associated with occupational exposures which involve much higher benzene concentrations than are encountered in the general environment. Most occupational exposures are presented as 8 hour time weighted averages (TWAs), and exposures outside the working day are not considered. Furthermore, few of the occupational studies include exposure data for women or for people over the age of 65 years. Studies in children are scarce. Several ecological studies have been conducted to examine adverse health effects associated with point sources from chemical plants.[14–17] Other studies have examined the association between car ownership, petrol combustion, and motor vehicle exhaust and leukaemia.[18] Exposure of fathers to benzene and other solvents before conception and postnatally has been associated with increased risk of childhood leukaemia.[19–21] However, none of these studies had quantitative estimates of benzene.

A summary of the health effects and estimated lowest observed adverse effect levels (LOAELs) for exposure to benzene are presented in table 1.

Acute toxic effects have usually been related to poor working conditions, accidents, or misuse and abuse of benzene. Inhalation of benzene produces acute toxic effects on the central nervous system in humans, which clear rapidly once exposure ends. Inhalation of 800–1600 mg/m^3 produces vertigo, drowsiness, headache, and nausea (table 1), whereas higher concentrations of 4800 mg/m^3 cause euphoria followed by giddiness, headache, nausea, staggered gait, and with continued exposure, unconsciousness.[22] Short term exposures to 9600 mg/m^3 can be tolerated for 0.5–1.0 hours. However, exposure to massive concentrations of 64 000 mg/m^3 or higher can be fatal within 5–10 minutes (table 1).

Table 1 Lowest observed adverse effect levels (LOAELs) in humans occupationally exposed to benzene

Effect	*Description*	*Exposure*	*LOAEL*	*Reference*
Acute toxicity:				
Death		Minutes	64000 mg/m^3	Thienes and Haley (1972)[82]
Death (oral*)			10 ml (8.8 g)	Thienes and Haley (1972)[82]
CNS	Vertigo, drowsiness, headache, nausea	Hours	800 mg/m^3	Clayton and Clayton (1994)[22]
Chronic toxicity:				
Haematological	Aplastic anaemia, pancytopenia	Years	320 mg/m^3	Yin *et al* (1987)[83]
				Greenberg *et al* (1939)[84]
	Myelodysplastic syndrome			Aksoy *et al* (1972)[85]
	Cytopenia	Years	96–112 mg/m^3	Fishbeck *et al* (1978)[23]
				Kipen *et al* (1989)[24]
				Rothman *et al* (1996)[25]
Mutagenic	Chromosomal aberrations	Years	64–319 mg/m^3	EBS (1996)[13]
	Adduct formation	Years	40–200 mg/m^3	Liu *et al* (1996)[26]
Carcinogenic	ANLL	Years	32–80 mg/m^3	Schnatter *et al* (1996)[48]
				Hayes *et al* (1997)[51]

ANLL=acute non-lymphocytic leukaemia; CNS=central nervous system.
*Only effect after oral consumption, all others resulting from inhalation.

Excessive repeated exposure to benzene (>320 mg/m^3) results in pancytopenia and aplastic anaemia, and is generally associated with a marked decrease in the number of cells in the bone marrow, resulting in severe clinical manifestations including immunosuppression and myelodysplastic syndrome. Lower repeated exposure to benzenes (<96 mg/m^3) results in cytopenia. Affected people may display a decrease in white blood cells potentially resulting in death due to infection, a decrease in platelet count potentially resulting in death due to haemorrhage, or a decrease in red blood cell count.[23–25]

Benzene is a known clastogen, causing chromosomal aberrations in vitro. The available data weakly suggest that prolonged exposure to long term mean concentrations of >64 mg/m^3 benzene may be associated with chromosomal aberrations.[13] Other reported indicators of genetic damage are sister chromatid exchanges, DNA cross linking, DNA adduct formation, and DNA repair. A study by Liu *et al*[26] found that both medium (40–200 mg/m^3) and high (>200 mg/m^3) concentrations of benzene resulted in significantly increased concentrations of the oxidative DNA adduct 8-hydroxydeoxyguanosine in workers at a shoe factory compared with a control group of university staff.

Benzene has long been known to be a human carcinogen, with the strongest evidence linking it with lymphohaematopoietic cancers, particularly acute non-lymphocytic leukaemia. Most of the evidence derives from industrial studies of workers exposed to benzene, often as a constituent of a complex mixture. These include the shoemaking, printing, petrochemical, chemical, coke production, and rubber manufacturing industries.[27–35] Many of the populations in these studies were exposed to benzene concentrations that were extremely high compared with concentrations experienced in these industries today.

There have been a few cohort and nested case-control studies that have estimated exposure information for each worker. Based on these studies, attempts have been made to develop dose-response relations with cumulative exposure—that is, assuming a symmetric contribution of concentration and duration of exposure. The cohort that has been most often used in risk assessment is the Pliofilm cohort, which included workers from three factories manufacturing rubber film in the United States. A wide range of exposures was encountered, with relatively few other chemicals involved. There have been several publications from this cohort giving mortality results[31 36–39] and risk assessments with different methods of estimating exposure and different mathematical models.[31 40–48]

The most recent follow up[49] reported 15 deaths from leukaemia, and estimated risks from three separate sets of exposure estimates.[37 44 45] The lowest exposure estimates were made by Rinsky *et al*[37] and the highest by Paustenbach *et al*[45]. Based on the exposure estimates of Crump and Allen[44] and Rinsky *et al*[37] excess risk for all leukaemia occurred at 160 mg/m^3 years, whereas based on the estimates of Paustenbach *et al*,[45] no risk occurred until a cumulative exposure of more than 1600 mg/m^3.years.

Four other cohort studies have measured exposure to benzenes for all their study subjects.[50–53] Bond *et al*,[50] in a follow up of a study by Ott *et al*[54] of 956 Dow chemical workers, found three deaths from leukaemia compared with 1.9 expected. Wong and Ott *et al*[53–55] followed up 7676 chemical workers, 3536 of whom were continuously exposed to benzene. Six deaths from leukaemia were reported in the exposed group compared with 4.5 expected. An update of a subgroup of this population has been reported by Ireland *et al*.[52] There were three cases of leukaemia found at exposures of 6 ppm (19.2 mg/m^3) or greater compared with 0.65 expected. Hayes *et al* reported[51] mortality results from a very large cohort of Chinese workers exposed between 1972 and 1987 in a variety of occupations. Excess risks were found for all leukaemias at all concentrations of exposure and above 40 ppm for acute non-lymphocytic leukaemia.

Two nested case-control studies have also been carried out on petroleum distribution workers[56 57] in which the method of retrospective quantitative estimation of exposures was essentially the same. No excess risk was found in any category of exposure in the study by Schnatter *et al*.[57] Of the 90 cases of leukaemia identified in the study by Rushton and Romaniuk,[56] 31 were acute myeloid and monocytic leukaemia (AMML). Risk from AMML did not increase with cumulative exposure analysed as a continuous variable. When categorised into discrete ranges an odds ratio of 2.8 was found (95% confidence interval (95% CI) 0.8 to 9.4) for a cumulative exposure of 4.5–45 ppm.years (14.4–144 mg/m^3.years) compared with <0.45 ppm.years (<1.44 mg/m^3.years).

A pooled analysis of the data from four studies[31 48 52 56] has been carried out[13] with several models. No dose-response pattern was found at concentrations of exposure below 1 ppm (3.2 μg/m^3). However, a cumulative exposure relation with acute non-lymphocytic leukaemia was suggested when concentrations were above about 20–50 ppm (64–164 μg/m^3).

Assessment of environmental exposure to benzene

Benzene has been reported in various matrices including air, fresh water and marine water, sediment, soil, foodstuffs, and organisms.[1] As benzene is primarily found in the atmosphere and human exposure is mainly through inhalation (95% of daily intake[39]) most monitoring programmes have concentrated on measuring concentrations in air.

AMBIENT AIR CONCENTRATIONS

Benzene has been routinely monitored in ambient outdoor air in the United Kingdom since 1991 as part of the automatic hydrocarbon monitoring network of the Department of the Environment, Transport, and the Regions.[58] Monitoring has also been carried out with passive monitoring networks. Tables 2 and

*Table 2 United Kingdom concentrations of benzene in outdoor air (μg/m³) for 1995 from the automatic hydrocarbon monitoring network**

Location	Site	Start date	1995 Mean concentration	Maximum hourly concentration	Data capture (%)
Middlesborough	Urban industrial	Jan 1993	3.5	139	95
London	Roadside	Feb 1993	5.4	60	91
London	Suburban	Mar 1993	3.2	49	91
Belfast	Urban background	Aug 1993	2.9	109	95
Birmingham	Urban background	Aug 1993	3.2	108	95
Edinburgh	Urban background	Aug 1993	2.2	36	90
Cardiff	Urban background	Nov 1993	3.8	78	86
Bristol	Urban background	May 1994	3.8	100	93
Harwell	Rural	Jan 1995	1.3	15.4	74
Leeds	Urban background	Jan 1995	3.2	76	94
Southampton	Urban centre	Sep 1995	8.0†	89	28
Liverpool	Urban background	Nov 1995	5.1‡	34	10

Values reported as ppb by the AEA.[6]
*Each monitoring station uses instruments which sample and analyse the ambient air continuously to provide levels of resolution.
†Mean concentration is a 4 monthly average as sampling was only conducted from September to December 1995.
‡Mean concentration is a 1 monthly average as sampling was only conducted during December 1995.
Concentrations for † and ‡ sites were not representative of the year as a whole as monitoring was not conducted for a whole year.

3 summarise recent United Kingdom data from these systems. Annual mean concentrations at urban sites (including suburban, city centre, and urban industrial) were in the range of 2.2–8.0 μg/m³. Data from a rural site showed a mean annual concentration of 1.3 μg/m³, which is about 30%–35% of the current concentrations measured at most urban backgrounds.[58] The running annual mean standard for benzene of 16 μg/m³ (5 ppb) recommended by the United Kingdom Expert Panel on Air Quality Standards (EPAQS) was not exceeded, although the EPAQS recommended target concentration for benzene of 3.2 μg/m³ (1 ppb) was exceeded at several urban sites.[59]

Similar results have also been found in the London area where much benzene monitoring has been carried out with diffusion tubes.[60] Benzene concentrations of as much as 118 μg/m³ have been reported at roadside sites close to the kerbside. Mean benzene concentrations at sites within 20 m of busy roads seem to cover the range 10–45 μg/m³. These concentrations are consistent with mean concentrations of 30–37 μg/m³ at the kerbside adjacent to roads with heavy traffic, estimated from measurements made at the Cromwell Road in London.[60]

There is a marked seasonal variation in outdoor air concentrations of benzene; in the winter they are about 1.5–3 times higher than during the summer,[58 61] possibly owing to the higher prevalence of cold still weather conditions at this time of year. Typical average concentrations in the Avon area for the period June 1991 to May 1992, for example, were 3 μg/m³ during the spring and summer and 5 and 8 μg/m³ during the autumn and winter months, respectively.[61]

INDOOR AIR CONCENTRATIONS

The Building Research Establishment (BRE) determined the concentrations of specific pollutants, including benzene, in a sample of 174 households of participants of the Avon longitudinal study of pregnancy and childhood in the Avon area.[62] The mean indoor concentration was 8 μg/m³ compared with an outdoor mean of 5 μg/m³. Higher concentrations of benzene in indoor air were associated with the presence of an attached garage, with the presence of a car kept in the garage being shown to result in an 80% increase in indoor air concentrations in the home.[61]

The BRE indoor environment study also reported a seasonal variation in indoor air concentrations which was due to the higher concentrations in the outdoor air which infiltrated the building, and the greater influence of indoor sources during winter compared with summer months, probably due to the lower rates of ventilation.[61]

Cigarette smoke has been found to contribute significantly to the concentrations of benzene reported in indoor air. The BRE study reported a significant increase in mean benzene concentrations in the living rooms of homes with one or more occupants who smoked compared with a non-smoking environment (9.6 μg/m³ compared with 7.2 μg/m³).[61] Another

Table 3 United Kingdom concentrations of benzene in outdoor air (μg/m³) from passive monitoring networks

Location	Sites (n)	Concentration	Comment	Reference
Urban, London	1	3.2–43.5*	Monthly average	EPAQS (1994)[59]
Outdoor, general†	59	1.6–7.04*	Mean ranges over 6 months	Downing *et al* (1994) [86]
Outdoor, Avon	13	5	Annual mean	Brown and Crump (1996)[62]
Roadside (<20 m)	NR	10–45*§	Averaging time not reported	DoE (1997)[60]
Semirural, Manchester	2	0.86–1.95*‡	Annual running mean	
Urban, Manchester	3	1.28–3.14*‡	Annual running mean	
Road side, Manchester	2	1.92–6.85*‡	Annual running mean	

NR=number of sites not reported.
*Values reported as ppb.
†This survey was conducted over a 6 month period in 1992 and measured various hydrocarbons at 59 sites with diffusion tubes.
‡Based on data supplied by Environmental Health Division, Technical Services Department, Manchester City Council, Town Hall, Manchester M60 2JT. Benzene monitoring has been conducted by Manchester City Council at seven locations since 1994. Data presented here are for the period January 1995–July 1997. The methodology involves passive sampling to obtain 2-weekly as well as annual running averages.
§Passive sampling with diffusion tubes.

study in the United Kingdom, conducted by Leung and Harrison,[63] reported higher daily exposures to benzene (active sampling over 12 hours during the day) for current smokers (23.0 μg/m^3) than for non-smokers (11.52 μg/m^3). Regular smoking (when smoking occurred every hour throughout the sampling period) led to increased concentrations of up to a maximum of 57 μg/m^3.

REFUELLING AND CONCENTRATIONS IN VEHICLES

Refuelling at petrol stations and exposure in vehicles have been shown to contribute to increased exposure to benzene. During refuelling, petrol station exposure varies according to the benzene content of fuel (usually, about 2%), the presence or absence of vapour control devices, and the amount of time spent at the stations. A detailed study has been conducted in Italy to determine the exposure of service station employees to benzene. (The results of the study, evaluation of exposure to benzene of employees and customers in filling stations of the AgipPetroli sector, were presented to a meeting held in Rome, Italy in February 1993. The data are available from AgipPetroli, Sede Centrale, Via Laurentina 449, 00142 Rome, Italy.) A total of 72 service stations were monitored throughout Italy covering motorway, suburban, and urban areas. The highest benzene concentrations were reported in the breathing zone of petrol station attendants, who were exposed to an average concentration of 482 μg/m^3. Fifty two per cent were exposed to an average of 320 μg/m^3, while 8% received maximum exposure concentrations in the region of 2000–3200 μg/m^3. Exposure varied widely, not only between different petrol stations, but also for the same petrol attendants at different times. Exposure to benzene was found to be related to the car type and pressure within the petrol tank and the ambient air.

The AgipPetroli study also showed that a single refuelling operation lasted about 1 minute, and that the mean air concentration to which the petrol attendant was exposed was 3709 μg/m^3, most of the benzene (88%) being emitted while supplying fuel to the vehicle. The introduction of vapour recovery systems was estimated to reduce the exposure of benzene emissions to 930 μg/m^3. An industrial hygiene subgroup of the Oil Companies' European Organisation for Environment, Health and Safety (CONCAWE) collated and summarised data from member companies on short term exposures (2–5 minutes) in the breathing zone of five service station attendants for the period 1986–92.[64] The mean air concentration was 2144 μg/m^3 with a range of 160–5200 μg/m^3 which seems to be in general agreement with the values reported for petrol attendants in the Italian study. This information, particularly the peak exposure during refuelling, can be used to derive exposure patterns for motorists in the United Kingdom who tend to self serve in filling stations.

Benzene found in the air inside vehicles is largely derived from engine exhaust emissions or evaporative losses, and varies in concentration according to the vehicle type and age, the fuel used, traffic variables, such as density and speed, and ventilation—that is, whether windows are open and ventilation fans or heaters are switched on.[65] Older vehicles tend to have slightly higher concentrations of vehicular pollutants than new vehicles. Slower average speeds, due to increased traffic, also tend to raise benzene concentrations inside the vehicle. At faster speeds there will be greater air turbulence, thereby diluting pollutant concentrations.[65] Similarly, concentrations seem to be lower with windows closed and vents opened and with windows closed and air conditioning on.[65] A mean in vehicle concentration of 55 μg/m^3 was reported for three BRE employees compared with an outdoor background concentration of 5 μg/m^3.[66]

CONCENTRATIONS OF BENZENE FROM OTHER SOURCES OF EXPOSURE

Benzene is not found in notable amounts in water, food, or consumer products. Freshwater, groundwater, and abstracted water concentrations generally have a mean concentration of benzene (range) of 0.64 (<0.1–35) μg/1, although in most samples (72%–100%), concentrations are below the detection limit.[67] Higher benzene concentrations of up to 12.5 mg/1 may be detected at contaminated sites.

As part of the total diet study, the Ministry of Agriculture, Fisheries and Food (MAFF) has measured benzene concentrations in foodstuffs in the United Kingdom. Mean benzene concentrations were 2.03 μg/kg of total food, with benzene being detected in most samples of carcass meat, offal, meat products, poultry, fish, and nuts, but not detected in most other food groups.[68]

As benzene is no longer permitted in products marketed to the general public, with the exception of petrol, any exposure from trace amounts in consumer products remaining in the home will be accounted for in measurements of indoor air.

RESULTS FROM PERSONAL AIRBORNE EXPOSURE MONITORING

The exposure of individual people to pollutants is dependent upon the time spent in a particular microenvironment and the concentration of the pollutant in that microenvironment. As people spend most of their time indoors, their exposure to benzene is strongly influenced by the concentrations of this compound in the indoor environment.[66] Exposure can also be enhanced by personal activities which result in higher concentrations in the breathing zone than in the general indoor environment—for example, through smoking.

The inhaled dose of benzene from cigarettes has been reported to be in the range 16–75 μg/cigarette.[69] Assuming an average of 40 μg/cigarette and assuming that 50% of inhaled benzene is absorbed or retained in the body, smoking 20 cigarettes/day would result in an inhaled amount of 800 μg/day and a retained dose of 400 μg/day.

With passive diffusion samplers, Mann *et al* (1997)[66] monitored the exposure of four BRE employees (all non-smokers) over a period of

12–30 months. The results, summarised in table 4, showed that mean personal exposure ranged from 7.3–11.0 μg/m^3. Highest exposure to benzenes were found in the garage, inside vehicles, and while riding a bicycle. Concentrations were lowest in the office and outside. With time activity data and concentrations of benzene in air in the different microenvironments, Mann *et al*[66] estimated that for individual people living in a non-smoking environment, the main exposure to benzene was through indoor air, owing to the high proportion of time spent in this microenvironment. Although only a short time (5%–8% of the day) was spent in a vehicle, exposure during transport was also relatively high, and resulted in 34%–44% of the total daily exposure to benzene.

In a larger study conducted by Leung and Harrison[63] active air sampling was used to monitor the personal exposure of 50 volunteers. In vehicle concentrations generally exceeded those measured at background outdoor locations (table 4) as did some of the indoor air concentrations. Personal exposures calculated indirectly from activity diaries and microenvironment measures (some of which are summarised in table 4) correlated well with those obtained directly from personal samplers. Personal exposures in the daytime (both urban and rural) were higher than at night (urban and rural). Increased exposures were experienced during refuelling and driving, especially in areas where dispersion was limited—such as in road tunnels and multistorey car parks. Exposure was further increased in volunteers who commuted during rush hours or travelled in congested traffic.

Estimation of typical daily intakes of benzene

Broadly, there are two ways of calculating a person's exposure to a substance. Firstly, individual exposure can be measured by personal monitoring over a typical period as they move between microenvironments. Secondly, typical concentrations in a relevant number of microenvironments can be measured and then be related to the time activity pattern of various subpopulations in each of those microenvironments.

The daily intake of a compound is the amount directly taken into the body by inhalation and ingestion of food and water. A summary of typical concentrations and doses of benzene for the key environment compartments is presented in table 5 on the basis of the information in these sections. As the contribution that food and water ingestion make to overall daily intake of benzene is likely to be very small, only exposure through inhalation has been considered. The value of 4 μg/m^3 for outdoor urban air is the mean of the figures for the nine urban sites presented in table 2 and the roadside value is derived from the mean for the London study.[60] The figures for refuelling were taken from the study by AgipPetroli (1995). Based on data presented for concentrations in vehicles, a value of 11 times the average urban concentration of 4 μg/m^3 is thought to be representative of typical exposure while driving and therefore typical in vehicle concentration can be assumed to be 44 μg/m^3. The figures for indoor concentrations in homes were taken from Crump.[61]

The daily exposure through inhalation can be calculated by multiplying the daily amount of air inhaled by the benzene concentration measured in each microenvironment—for example, concentration in the work place, in vehicles, home, or outdoors—by the fraction of time spent in that microenvironment, estimated from time activity surveys. These, in conjunction with appropriate inhalation and absorption rates, can then be used to estimate exposure to benzene for various subpopulations of the non-occupationally exposed general population.

TIME-ACTIVITY DATA

In northern European countries, people spend a large proportion of their time indoors (about 90%–95%), and much of this time is in the home.[66] Although no in depth studies have been conducted in the United Kingdom to determine time-activity patterns for the general

Table 4 Benzene concentrations (μg/m^3) measured by personal and fixed site monitors for two United Kingdom studies

	*BRE study**		*Birmingham study†‡*			
Study location	*Employees (n)*	*Range of means*	*Observations (n)*	*Mean*	*SD*	*Range*
Living room§	4	5.5–7.2	15	11.52	2.24	—
Main bedroom	4	8.5–17.8	—	—	—	—
Smoky pub	—	—	16	79	21.12	—
Outside	3	2.9–7.3	15	14.08	2.24	—
Pedestrian area	—	—	15	18.24	2.88	—
In vehicle	3	19.0–80.3	52	41.3	34.9	—
On bicycle	1	16.1	15	12.48	4.16	—
Office	4	3.5–5.0	—	—	—	—
Refuelling	—	—	15	190	155	—
Garage	1	144.7	—	—	—	—
Personal exposure:						
Annual mean	4	7.3–11.0	—	—	—	—
12 h daytime exposure	—	—	50	12.2	—	0.74–283
12 h night time exposure	—	—	—	6.2	—	1.95–18

*Data from Mann *et al*[66]; sampling at fixed locations was for consecutive 28 day exposure periods.
†Data from Leung and Harrison[63]; microenvironment sampling periods were between 10 and 30 minutes. Outside refers to Birmingham city centre.
‡Values reported as ppb in original papers.
§Non-smoking house.

Table 5 Summary of typical environmental concentrations for the United Kingdom

Media	*Concentration*	*Comment*
Air:		
Outdoors, rural	1.3 μg/m^3	
Outdoors, urban	4 μg/m^3	
Roadside	33 μg/m^3	Adjacent to heavy traffic road
During refuelling	3700 μg/m^3	No evaporative emission control installed
During refuelling	930 μg/m^3	Evaporative emission control installed
In vehicle*	44 μg/m^3	11 Times concentrations of background urban sites
Indoors, rural no smokers†	5 μg/m^3	
Indoors, urban no smokers†	7 μg/m^3	
Indoors, 1 or more smokers†	10 μg/m^3	
Active smoking	800 (400) μg/day	Average daily exposure (and retained dose) assuming that 20 cigarettes are smoked a day, each containing 40 μg of benzene and that 50% of inhaled benzene is absorbed
Other compartments:		
Drinking water	0.64 μg/1	
Foodstuffs	2.0 μg/kg	Average concentrations in food
Soil	Trace amounts	
Consumer products	Trace amounts	
Dermal	Trace amounts	

*Concentrations are assumed to be similar while using public and private transport as no information is available for concentrations in buses. If the main form of transport is by rail, this value is likely to over estimate actual concentrations; Leung and Harrison[63] have shown levels in trains to be lower than in vehicle concentrations.
†Owing to lack of monitoring data in other indoor areas—for example, offices, schools, etc—it is assumed that concentrations in these areas are similar to those reported in the home.

population, there are a few studies that report this type of information for specific population groups. For the purpose of this assessment, time activity has been subdivided into (*a*) 91% spent indoors (home, office, or elsewhere), (*b*) 5% spent in transport (public or private), (*c*) 2 minutes a week spent refuelling (not children or infants), and (*d*) 4% spent outdoors.[7] For the purpose of this paper it has been assumed that children and infants will not be exposed to benzene from refuelling. Although they are unlikely to be adjacent to the petrol pump or petrol tank during refuelling, it is possible that exposure inside the vehicle might increase during this procedure. However, no reliable data exist with which to estimate this. For smokers, a daily dose of 400 μg/day from cigarettes has been assumed.

INHALATION AND ABSORPTION RATES

An average inhalation rate of 20 m^3 air/day and an absorption rate of 50% has been assumed for estimating the human absorbed dose of benzene through inhalation.[7] This inhalation rate value is widely used to determine the inhaled dose for a given air pollutant for adults. Children have much lower inhalation rates; Layton[78] reported average inhalation rates for infants (<1 year old) and children (aged 1–10 years) of 4.5 and 8.6 m^3 per day, respectively.

Table 6 Estimated absorbed daily doses of benzene (μg/day) for members of the general public under different exposure scenarios

Activity	*Rural non-smoker (a)*	*Urban non-smoker (b)*	*Urban passive smoker (c)*	*Urban smoker (d)*	*Extreme case (e)*
Indoors	45.5	63.7	91	91	58
In vehicle	22	22	22	22	22
Refuelling*	1.9–7.4	1.9–7.4	1.9–7.4	1.9–7.4	1.9–7.4
Outdoors, pleasure	0.5	1.6	1.6	1.6	1.6
Outdoors, work†	—	—	—	—	330
Smoking	—	—	—	400	400
Total daily dose	70–75	89–95	116–122	516–522	814–819

*The lower of the reported range refers to whether vapour recovery equipment has been fitted in filling necks and petrol pump nozzles. As these are still not required by United Kingdom or European Union legislation, the higher value of this range will reflect current exposure more accurately and therefore this value is used for evaluating benzene exposure to the general United Kingdom population. As the Department of the Environment, Transport and the Regions is preparing a consultation paper for a scheme to implement controls to reduce emissions from this source, there should be a gradual reduction of exposure to benzene from this source (down to an estimated daily absorbed dose of 1.5 μg) over the next few years.
†Breathing rate for heavy activity is 2.5 m^3/h (Layton[78]).

Human exposure estimates with different exposure scenarios

Using these time-activity patterns and inhalation and absorption rates, in conjunction with measured benzene air concentrations for each microenvironment, absorbed daily doses for the United Kingdom general adult population have been estimated for five scenarios (table 6).

(*a*) Non-smoker who lives in a rural environment.

(*b*) Non-smoker who lives in an urban environment.

(*c*) Non-smoker who lives in an urban environment in a house where at least one member of the family smokes.

(*d*) Smoker who lives in an urban environment.

(*e*) Smoker who spends 8 hours/day actively working close to heavy traffic—for example, road workers on a busy city-centre road.

The absorbed daily dose for a rural non-smoker, although indoors is calculated, for example, by multiplying the typical indoors concentration for a rural non-smoker from table 5 (5 μg/m^3), the proportion of time spent indoors (0.91), the mean inhalation rate (20 m^3), and the absorption rate (0.50) to give 45.5 μg/day. Similar calculations have been made for the other three time activities for this scenario—namely, time spent in vehicles, refuelling, and outdoors—and these four calculations have been summed to give the total daily dose for a rural non-smoker of 70–75 μg/day .

Thus, the estimated mean absorbed doses of benzene to which the general population are exposed through air in non-smoking environments are estimated to be in the ranges 70–75 μg/day and 89–95 μg/day, for rural and urban residents, respectively (table 6). Rural residents are exposed to lower concentrations owing to the lower indoor air concentrations. Table 6 shows that active smoking can contribute four times the dose obtained from all other sources.

Table 7 Estimated benzene absorbed daily doses (μg/day) for infants and children under different exposure scenarios

Activity	*Rural infant (f)*	*Urban infant (g)*	*Urban infant passive smoker (h)*	*Rural child (i)*	*Urban child (j)*	*Urban child passive smoker (k)*
Indoors	10.2	14.3	20.5	19.6	27.4	39.1
In vehicle	5.0	5.0	5.0	9.5	9.5	9.5
Outdoors, pleasure	0.1	0.4	0.4	0.2	0.7	0.7
Total daily dose*	15.3	19.7	25.9	29.3	37.6	49.3

*Note that because of rounding total daily dose may not add up to last decimal place.

Table 8 Summary of estimated absorbed doses of benzene for adult members of the general public under different exposure scenarios

	Daily dose (μg/day)	*Daily intake (μg/kg bw/day*)*		*Equivalent atmosphere concentration† (μg/m³)*
		Women	*Men*	
Rural non-smoker	75	1.29	1.07	3.75
Urban non-smoker	95	1.64	1.36	4.75
Urban passive smoker	122	2.10	1.74	6.10
Urban smoker	522	9.00	7.46	26.10
Urban smoker who works adjacent to busy road for 8 h/day	819	14.12	11.70	41.95

*Values converted from daily doses by assuming that the average United Kingdom woman and man weigh 70 and 58 kg, respectively.[7]
†Values converted from daily doses by assuming that the average person inhales 20 m^3 of air per day.

Exposure to benzene will be higher for people who spend a large proportion of their day near city centres and congested roads, especially when involved in high levels of physical activity (as this will increase their inhalation rate and therefore intake of benzene from air). An example of such a situation is presented in scenario (*e*) where a person who smokes 20 cigarettes/day and works 8 hours/day in an active job—for example, a labourer—adjacent to a busy city centre road, may be exposed to an absorbed dose of 819 μg/day (table 6).

Table 7 presents estimates for infants (<1 year old) and children (aged 11 years) for similar scenarios:

(*f*) An infant who lives in a rural environment.

(*g*) An infant who lives in an urban environment.

(*h*) An infant who lives in an urban environment in a house where at least one member of the family smokes.

(*i*) A child who lives in a rural environment.

(*j*) A child who lives in an urban environment.

(*k*) A child who lives in an urban environment in a house where at least one member of the family smokes.

Infants and children living in rural areas receive around half the daily absorbed dose of benzene (15.3 μg/day and 29.3 μg/day, respectively) of those living in cities (19.7 μg/day and 37.6 μg/day). Attention is drawn to the increase in dose received by infants and children through passive smoking.

Tables 8 and 9 present the daily doses (μg/day), from table 6 and 7, respectively expressed as daily intakes (μg/kg body weight/day), and as mean daily inhaled dose—that is, the atmospheric concentration to which a person would have to be exposed every day to achieve the daily dose, the "equivalent atmospheric concentration" (μg/m^3). The upper point of the ranges for adults have been used. Values were converted from daily doses to daily intakes by assuming that the average infant (<1 year old) weighs 9.1 kg, the average child (age 11 years old) weighs 41.1 kg, and the average man and woman weigh 70 and 58 kg, respectively. These may not be representative of the whole United Kingdom population, but have been used to give an estimate of exposures in typical people. Similarly values were converted from daily doses to equivalent atmospheric concentration by assuming that the average infant, child, and adult inhales a volume of air of 4.5, 8.7, and 20 m^3/day, respectively. The atmospheric concentrations are particularly useful estimates, as the limit values, whether environmental or occupational, for substances which are principally encountered as airborne contaminants, are expressed in such units. Thus, risk management procedures, should they be thought necessary at any stage, can use the figures, the typical microenvironment concentrations, time-activity patterns, as well as emission concentrations and make risk reduction recommendations based on real information.

Table 9 Summary of estimated absorbed doses of benzene for infants and children under different exposure scenarios

	Daily dose (μg/day)	*Daily intake (μg/kg bw/day*)*	*Equivalent atmospheric concentration† (μg/m³)*
Rural infant	15.3	1.68	3.40
Urban infant	19.7	2.16	4.38
Urban infant, passive smoker	25.9	2.55	5.76
Rural child	29.3	0.71	3.37
Urban child	37.6	0.91	4.32
Urban child, passive smoker	49.3	1.20	5.67

*Values converted from daily doses by assuming that the average infant (<1 year old) weighs 9.1 kg and the average child (11 years old) weighs 41.1 kg; there will be a progression in ranges so that on average a 1 year old weighs 11.3 kg, a 5 year old weighs 19.7 kg, an 8 year old weighs 28.1 kg, and so on.
†Values converted from daily doses by assuming that the average infant and child inhales a volume of air of 4.5 and 8.7 m^3/day respectively.

Table 9 shows that infants and children receive a mean daily dose of 15.3–25.9 and 29.3–49.3 μg/day, respectively, equivalent to a mean atmospheric concentration of 3.4–5.76 μg/m^3 and 3.37–5.67 μg/m^3. It is worth noting that infants and children exposed to environmental tobacco smoke have concentrations of exposure to benzene comparable with those of an adult passive smoker (table 8). The potential consequences of exposure to benzene

in infants may be more important than equivalent exposure for children or adults owing to their lower body weight; this is reflected in their higher daily intake (1.68–2.85 μg/kg bw/day) in comparison with children (0.71–1.20 μg/kg bw/day) or non-smoking adults (1.07–2.10 μg/kg bw/day). The worst case scenario for exposure to benzene in the general population is that of an urban smoker who works adjacent to a busy road for 8 hours/day—for example, a maintenance worker. This person's average daily exposure would be about 42 μg/m^3 (table 8). Such a scenario represents a physically active person whose inhalation rate would be higher than that of a person in a more sedentary occupation.

Comparison of the estimated absorbed dose of benzene for adults, infants, and children (tables 8 and 9) with the LOAELs (table 1) shows that concentrations to which the general population in the United Kingdom are exposed are well below all the reported LOAELs, in fact, three orders of magnitude lower than the estimated LOAEL for acute non-lymphocytic leukaemia.

Discussion

Most assessments of the potential adverse health effects of benzene have focused on occupationally exposed workers, in particular men. In attempting to evaluate the potential effect of environmental concentrations of benzene, this assessment has had to make many assumptions, depending on the availability and quality of data on exposures, health effects, and population characteristics.

The concentrations of outdoor benzene in the United Kingdom summarised in this paper are within the ranges reported elsewhere. Recent large scale studies in the United States and Canada, for example, have shown that mean outdoor air concentrations are in the range 1–8 μg/m^3.[39] In The Netherlands, studies have shown that in streets where cars are parked, concentrations of benzene indoors and at the front of houses can be 1.5–2 times higher than those measured at the back of the houses.[70] This has been attributed to the evaporation of benzene from petrol tanks and engines. This source of benzene is likely to be as important in the United Kingdom as highlighted by the higher benzene concentrations reported near busy roads.

The values of indoor concentrations also seem to agree with those reported from other countries.[39] In particular, the results showing the influence of an attached garage in increasing indoor air concentrations of benzene have also been found in studies in the United States.[71] In the United Kingdom study by Brown and Crump[62] 22% of houses had an attached garage, which, if typical, may indicate that this factor could affect a substantial proportion of the United Kingdom population.

Factors such as the number of smokers per household, how many cigarettes are smoked each day, and household characteristics such as room size and ventilation rates have been shown to influence exposure in the home.[71] The fact that in 1995, in the United Kingdom, a mean of 29% of men and 27% of women were current smokers and that 47% of children (2–15 years) lived in households with at least one person who smoked[72] highlights the importance of this source of indoor air exposure to benzene.

Various large scale studies from other countries have also highlighted the contribution that cigarette smoke makes to concentrations of benzene in indoor air. The United States total exposure assessment methodology (TEAM) studies have reported median concentrations of benzene in 200 homes without smokers to be 7 μg/m^3 compared with 10.5 μg/m^3 in 300 homes with one or more smokers.[73] Measurements in 230 homes in West Germany found very similar results, with median values of 6.9 μg/m^3 in no-smoking homes and 9.3 μg/m^3 in homes with smokers.[74]

In the United Kingdom, vehicle refuelling is mainly carried out by the customer. Under a proposed Stage II of the Petrol Vapour Recovery Directive 94/63/EC (PVR; EEC, 1994; OJ L365 31.12.1994), benzene emissions from petrol pumps were to be reduced by 70% by the year 2006. The European Union is no longer taking this directive forward. However, the Department of the Environment, Transport and the Regions is currently planning to implement a similar scheme. By taking into account the variety in shape of vehicle tank caps, erroneous manoeuvres by petrol attendants, accidental dysfunction of the system, and so on, the AgipPetroli study of service station employees estimated that the introduction of vapour-recovery systems would be capable of reducing the exposure of benzene emissions by 80% during "fuel in flow" and by 50% during removal and replacement of the nozzle and closure of the vehicle tank. This would reduce air concentrations during refuelling from 3709 μg/m^3 to 920 μg/m^3.

Concentrations in vehicles reported in the United Kingdom studies are within the range of those reported elsewhere, which have generally found that mean exposure to benzene in vehicles can be in the order of three to 10 times greater than the background ambient concentrations.[39] A recent Australian study reported benzene concentrations inside new cars as being around 11 times higher than ambient concentrations.[75] This value was even higher for older cars without catalytic converters, where concentrations in vehicles during city driving were 27 times higher that ambient background concentrations, although concentrations dropped sharply in faster flowing motorway traffic. In general, concentrations in vehicles were about twice as high for cars without catalytic converters than for newer models with catalytic converters. This study showed that the pollution inside cars was a result of a combination of the cars' own exhaust emissions and those from the other vehicles on the road.

In general, studies in the United Kingdom of the relation between simultaneous measurements of outdoor, indoor, and personal levels of exposure have shown that mean personal air concentrations exceed indoor air concentra-

tions, which in turn exceed outdoor air concentrations. Results obtained in the two United Kingdom studies[63 66] are in the range of those reported in the United States (3.2–24 μg/m^3).[39] The mean personal exposure was about 15 μg/m^3 with a range of 7–29 μg/m^3. They also found that the overwhelming source of exposure to benzene for smokers was mainstream cigarette smoke. Smokers have a mean benzene body burden of about 6–10 times that of non-smokers and receive about 90% of their exposure to benzene from smoking.[39] In this paper, our assumptions give a figure of around 77% for the contribution from smoking. For non-smokers, most exposure to benzene was ultimately derived from vehicle exhaust or petrol vapour emissions, with a portion of exposure (10%) being due to environmental tobacco smoke.

The calculation of absorbed daily doses was based on typical benzene concentrations in relevant microenvironments, time-activity patterns, and inhalation and absorption rates. Typical average figures from published studies have been used for time spent indoors, outdoors, and travelling. However, these are known to vary by such factors as age, sex, and employment. Infants and elderly people spend proportionately more time indoors than school age children and adults. Patterns also vary by day of the week and season, with more time generally spent outdoors during the summer months.

Average inhalation and absorption rates were used in this assessment. However, breathing rates are affected by numerous individual characteristics, including age, sex, weight, health, and level of physical activity (running, jogging, etc). Daily inhalation rates may also vary with exposure to lower environmental concentrations of benzene. Inhalation rates may be higher among outdoor workers and athletes because levels of activity outdoors may be higher. Therefore these population groups may be more exposed to air pollutants than the general population and could be considered to be high risk groups.[76 77] Mean inhalation rates of 0.2 m^3/hour have been estimated for periods of rest, and 0.3, 0.5, 1.0, and 2.5 m^3/hour for sedentary, light, moderate, and heavy levels of activity, respectively.[78]

The absorbed daily doses were calculated for several scenarios. The estimated values are within the same range as those reported elsewhere in Europe. Oil Companies' European Organisation for Environment, Health and Safety,[79] for example, estimated absorbed doses of 74 μg/day for non-working, non-smoking, non-driving residents in a rural environment and up to 458 μg/day for office workers who smoke, drive, and live in an urban environment. Similarly, the United Kingdom Expert Panel on Air Quality Standards[59] estimated daily intakes ranging from 120 μg for a non-smoker living in an unpolluted rural area to 1250 μg/day for a smoker living in a city.

The most significant potential adverse health effects from prolonged, low level exposure to benzene are haematotoxicity and carcinogenicity. Most quantitative risk assessments have been conducted with leukaemia as an end point as this is the most serious health risk associated with prolonged, occupational exposure.

The LOAEL for leukaemia for workers occupationally exposed to benzene has been estimated to be 32–80 mg/m^3. However, because benzene is considered to be a genotoxic carcinogen, a safe or no effect level cannot be identified. Therefore many studies have used quantitative risk assessments or modelling to extrapolate from occupational exposures to estimate the risk to health from low level exposure to benzene.

It is important to note that there is continuing debate about the appropriateness of risk assessment with mathematical modelling. Also, the underlying mechanisms by which benzene causes cancer is not clearly understood, nor is it known whether the leukaemogenesis is related to average steady state or intermittent high peak exposure. Quantitative risk assessment with the linearised multistage model often used for carcinogens has been seriously challenged as unreliable and scientifically unsound,[80] and the United Kingdom Committee on Carcinogenicity of Chemicals in Food, Consumer Products, and the Environment, for example, does not support the routine use of quantitative risk assessment for chemical carcinogens. Maynard *et al*[81] proposed an alternative approach for the purpose of setting air quality standards and recommended a strategy based on the scientific data, decision points and uncertainty factors. Thus, although this review has presented the currently reported risk estimates for leukaemogenesis associated with benzene as the appropriate risk estimates for adverse health effects from low level exposure to benzene, it is possible that these estimates will change as the mechanism for carcinogenesis is further elucidated and more appropriate models, based on mechanistic considerations, emerge.

As previously noted almost all studies of the potential adverse effects of exposure to benzene have been carried out on adult male workers. Occupational exposure usually pertains to an 8 hour day, 5 days a week, for about 50 weeks a year, for 40–45 years, whereas continuous exposure among the general population covers 24 hours a day, 7 days a week, for 52 weeks a year, for about 70 years. None the less, even for a worst case scenario, environmental exposure to benzene is several orders of magnitude lower than the lowest occupational exposures associated with adverse health impacts. Moreover, over the past 30 years car use and petroleum consumption has risen drastically. This has not been accompanied by an increased incidence of leukaemia.

It is always possible that some sectors of the population might be more susceptible to leukaemia induced by benzene. Children may be of particular concern; it could be argued that children's blood cells are dividing and maturing more rapidly, which could produce enhanced susceptibility to an environmental agent capable of causing leukaemia. However, the most prevalent type of leukaemia in children is acute lymphocytic leukaemia as

opposed to acute myeloid leukaemia, the type which has been most strongly linked to exposure to benzene. In the United Kingdom, of the 66 children under 15 who died of leukaemia in 1995, 41 (62%) died of acute lymphocytic leukaemia and 17 (25%) died of acute myeloid leukaemia.[68] Furthermore, it is also important to recognise that some of these leukaemias may be the result of exposure to radiation and viral infections, proved aetiological factors.

Conclusions

The major health risk associated with low level exposure to benzene is leukaemia and the strongest link in humans has been associated with acute non-lymphocytic leukaemia. To date few data have been found relating adverse health effects among women, children, or elderly people to exposure to benzene, as most studies have involved exposure of male workers. The lowest level of exposure at which an increased incidence of acute non-lymphocytic leukaemia among occupationally exposed workers has been reliably detected seems to be in the range of 32–80 mg/m^3. Although some studies have suggested that effects may occur at lower concentrations, clear estimates of risk have not been assessed, partly because of the inadequacy of exposure data and the few cases. Overall, the evidence from human studies suggests that any risk of leukaemia to adults at general population continuous exposure concentrations of 3.8 to 42 μg/m^3, which have been derived from available United Kingdom exposure data—that is, it is at concentrations three orders of magnitude less than the occupational lowest observed effect level—is likely to be exceedingly small and probably not detectable with current methods. The same approach applies for infants and children who may be exposed continuously to concentrations of 3.4–5.7 μg/m^3. As yet there is no evidence to suggest that continuous exposure to environmental concentrations of benzene manifests as any other adverse health effect.

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Answers to multiple choice questions

(1) (a) True (b) True (c) False (d) False (e) True
(2) (a) False (b) True (c) False (d) True (e) False
(3) (a) False (b) False (c) True (d) True (e) False
(4) (a) False (b) True (c) True (d) True (e) False
(5) (a) False (b) False (c) False (d) True (e) False